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4 April 00 — Colby S. Delgado
Date — Colby S. Delgado

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Lars Abrahmsen, et al.

Filed: July 25, 1997

Serial No.: 08/765,695

For: CONJUGATE BETWEEN A MODIFIED SUPERANTIGEN AND A TARGET-SEEKING COMPOUND AND THE USE OF THE CONJUGATE

§

Atty. Docket: P01525US0 / 09804877

Group Art Unit: 1644

Examiner: R. Schwadron

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SUBSTITUTE PETITION TO THE COMMISSIONER UNDER 37 C.F.R. § 1.181 FROM IMPROPER REQUIREMENT FOR RESTRICTION

Applicants respectfully Petition the Commissioner under the provisions of 37 C.F.R. § 1.144 and 1.181 for withdrawal of an improper requirement for restriction pending in the above-referenced case. This is a Substitute Petition to the original Petition filed November 15, 1999 and is in response

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to an Office Communication mailed February 11, 2000 in which the Examiner commented on the restriction issue and suggested that a Substitute Petition be filed to address the comments.

As explained below, the Examiner is maintaining the restriction requirement on the ground that, allegedly, independent claim 14[1/] of the case as filed are not patentable over the prior art (Buelow et al., in particular) and therefore restriction is proper under MPEP Section 1850 (July 1998, 1800-51). Applicants assert that all the independent claims as filed are patentable over the prior art, therefore unity of invention is present, and the restriction requirement should be withdrawn.

Statement of Facts

The above-captioned patent application bears a United States Patent and Trademark Office filing date of July 25, 1997. Claims 14-51 were initially pending. On October 16, 1998 a Restriction Requirement was issued which defined Group I claims (14-35) as being drawn to a conjugate and Group II claims (36-51) as being drawn to a method of treatment using the conjugate. The independent claims as filed are:

Group I:

14. A conjugate comprising:

a. a biospecific affinity counterpart that is capable of binding to a surface structure, and

b. a peptide that

[1/]In the Office Communication of February 11, 2000 the Examiner referred to claim 1 as a restricted independent claim covering the conjugate. However, we presume the intent was to refer to claim 14, as there is no pending claim 1, and restricted claim 14 is an independent claim covering the conjugate.

i. contains an amino acid sequence that is derived from a superantigen,

ii. has the ability to bind to a Vβ of a T cell receptor, and

iii. has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived,

which parts are covalently linked together.

Group II:

36. A method for the treatment of a diseased condition in a mammal, which condition means the presence of specific cells that are associated with the condition by the expression of a disease specific cell surface structure, wherein one administers to the mammal a therapeutically effective amount of covalent conjugate that is able to activate T lymphocytes to lyse cells that carry the disease specific cell surface structure and comprises:

a. a biospecific affinity counterpart that is capable of binding to said surface structure, and

b. a peptide that

i. contains an amino acid sequence that is derived from a superantigen,

ii. has the ability to bind to a Vβ of a T cell receptor, and

iii. has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived.

The restriction requirement was based upon the Examiner's assertion that the special technical linking feature of the groups, the conjugate of Group I, was allegedly not patentable over Buelow et al. (J. Immunol., 1992, 148:1-6).

On November 16, 1998 applicants responded to the restriction requirement with traverse, provisionally electing claims of Group II. Reconsideration of the restriction requirement was requested.

On August 16, 1999 a first substantive Office Action was issued on the case. (Applicants note with concern that the first substantive examination in the case was not issued until more than two years following the U.S. filing date of the application). In that Office Action the Examiner maintained and made Final the restriction requirement based upon the same grounds, the alleged unpatentability of the independent claims over Buelow.

On November 15, 1999, an Amendment and Response was filed in response to the Office Action of August 16, 1999, and the original Petition to the Commissioner under the provisions of 37 C.F.R. § 1.144 and 1.181 for withdrawal of an improper requirement for restriction was filed in the case.

On February 11, 2000 the Examiner issued an Office Communication adding additional comments to support the restriction requirement and suggesting that Applicants file the present Substitute Petition to address the new comments.

Point For Review

Applicants respectfully submit that the restriction requirement is improper because the independent claims are patentable over the prior art and thus all claims as filed should be examined in a single application as required under PCT Article 3(4)(iii) and 17(3)(a), PCT Rule 3.1, 37 C.F.R. § 1.475, and MPEP Section 1850.

Arguments

The Examiner is basing this Restriction Requirement upon the position that the independent claims are allegedly not patentable over Buelow, et al., J. Immunol., 1992, 148:1-6, because Buelow, allegedly, inherently discloses the subject matter of the special technical feature and independent claim 14. The is incorrect because Buelow is not an enabling disclosure of the inventive subject matter (the special technical feature/the conjugate of independent claim 14) and therefore does not anticipate the subject matter.

The Examiner had originally based the restriction upon an incorrect interpretation of Buelow, wherein it was asserted that Buelow taught that a protein A-SEB conjugate wherein the SEB of the conjugate only contains amino acids 1-130 of SEB had activity. As argued in the first Petition, filed in November 1999, this is not a correct interpretation of Buelow as the fragment of 1-130 amino acids of Buelow does not have activity.

The Examiner then changed the basis of the restriction in the Office Communication filed February 11, 2000 and noted that a fragment having amino acids 1-138 in Buelow has activity, and therefore averred that, allegedly, Buelow inherently anticipates the inventive subject matter.

Applicants respectfully disagree. The special technical feature, the conjugate of claim 14, involves a superantigen conjugate in which the superantigen has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived. Buelow does not anticipate the inventive subject matter (the special technical feature and claim 14) because it is not an enabling disclosure of the inventive subject matter. In order to anticipate, prior art must provide an enabling disclosure of the anticipated subject matter. Here, the alleged anticipated subject matter is drawn to a superantigen conjugate in which the superantigen has been mutated to show a modified ability to bind to MHC class II antigens compared to the superantigens from which the peptide is derived. Enablement for such a conjugate requires guidance as to, for example, which regions of the superantigen to mutate (and, for example, how to mutate them) and which particular "modified" abilities to bind MHC class II antigen to expect therefrom.

Buelow does not in any manner teach, disclose or suggest mutating residues in a full length superantigen in order to affect (modify) MHC Class II antigen binding. It is entirely unclear from Buelow which regions of a full length superantigen should be mutated in order to expect a mutant protein with altered MHC Class II binding. The disclosure, teaching and suggestion of Buelow all are directed solely to the *use of truncated pCA-SEB fusion proteins to map to the amino-terminal half of the molecule (residues 1-138) a minimally immunologically active domain of SEB capable of inducing proliferation and anergy in cloned human T cells expressing VB3.1* (see first paragraph of page 2, Buelow). Buelow is not aimed at identifying the MHC Class II binding domain and certainly is not aimed at identifying which residues of full length superantigens may be mutated to specifically alter Class II MHC antigen binding. Buelow provides an indication that the region encompassing residues 1-138 of SEB constitutes a functional (i.e., "immunologically active")

domain of the molecule; however, the Buelow authors recognize that it remains to be determined which parts of the molecule are involved in the interactions with Class II MHC antigens and TCR molecules, for example, directly, and/or indirectly (for example by influencing the conformation of the molecule) (see Discussion section on page 6, Buelow).

Indeed, the actual data presented in Buelow makes it clear that it does not teach or predict anything about Class II MHC antigen binding. For example, F45 and E67 are known to be important for Class II MHC binding in SEB and both the Buelow 1-130 and 1-138 SEB fragments have these identical (wild-type) sequences. However, as discussed above and plainly shown in Buelow, these two proteins have dramatically differing activities; the fragment 1-130 has neither mitogenic nor tolerogenic activity, while 1-138 fragment (identical *but for* the additional eight amino acids which are not in the recognized Class II MHC binding region) has activity. Hence, there is no way that one skilled in the art could gain any information from Buelow about which residues in superantigens are important in Class II MHC binding.

Applicants, therefore, respectfully assert that all claims as originally presented and currently pending (claims 14-38, 44-47 and 52-57) are patentable as a single invention.

Action Requested

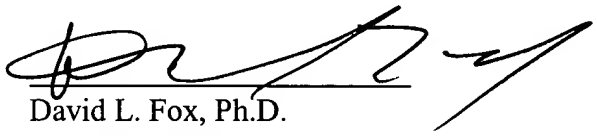
In light of the above-noted facts, and arguments, applicants respectfully request that the presently pending restriction requirement be withdrawn and all claims as filed and presently pending (claims 14-38, 44-47 and 52-57) be examined on the merits in the above-noted patent application.

Fees Paid

Please charge any fees due for this Petition to the standing account of Fulbright & Jaworski L.L.P., Deposit No. 06-2375/09804877.

Applicants respectfully petition for any extension of time necessary to render this response timely.

Respectfully submitted,



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